

### REMARKS

In the Office Action of May 29, 2001, Claims 6 - 17 were rejected. No Claims was allowed. In response, Claims 6, 10 and 14 are amended. Reexamination and reconsideration are respectfully requested in view of the following remarks.

#### Request for Entry of Amendments

Applicants hereby request that the amendments presented herein be entered in the application under 37 CFR 1.116. The amendments presented herein simplify the issues for consideration and thereby place the claims in better form for allowance or appeal. In particular, applicants have amended the claims to limit the heterocyclic groups in the definition of  $R_5$  and  $R_6$  of formula (I) to specific groups.

Support for the amendments to Claims 6, 10 and 14, particularly for the definition of heterocyclic groups is found on pages 4 and 5 of the specification.

#### Objection to the Claims

Claims 6, 10 and 14 were objected to on the grounds that the recitation "wherein n is an integer of 0 to 4" should follow the complete formula  $-(CH_2)_n-R_5$ . This correction is made in the amendments presented herewith.

**Rejection of Claims 6 - 17 under 35 U.S.C. §112, first paragraph**

In the previous Office Action, Claims 1 - 5 were rejected under 35 U.S.C. §112, first paragraph on the alleged grounds that the specification, while being enabling for exhibiting the pharmacological activity of inhibition of neurodegeneration following the application of four test compounds, as disclosed in Table 2, page 12, does not reasonably provide enablement for compounds of formula I wherein any heterocyclic group is attached. In the present Office Action, the Examiner stated that the rejection is maintained, but that favorable consideration would be given to the limitation of the heterocyclic groups in Claims 6, 10, and 14 to furyl and pyridyl. In response, Claims 6, 10, and 14 are amended to designate specific heterocyclic groups in the definitions of R<sub>5</sub> and R<sub>6</sub>. Accordingly, it is respectfully submitted the specification provides enablement for the compounds of Claims 6, 10 and 14 as amended, and that the rejection under 35 U.S.C. §112, first paragraph is thereby overcome.

**Rejection of Claims 6 - 17 under 35 U.S.C. §102(b) over Badger et al**

Claims 6 - 17 were rejected under 35 U.S.C. §102(b) as anticipated by Badger et al (U.S. Patent No. 4,772,607). The Examiner alleges that Badger teaches the administration of

compounds of formula 1, such as, for example when  $X_1$  and  $X_2$  are O,  $R_1$  and  $R_2$  are lower alkenyl,  $R_3$  is hydrogen  $R_4$  is  $O(CH_2)_n-R_5$  and  $R_5$  is phenyl substituted one to three times with hydroxy or alkoxy.

It is respectfully submitted that this rejection is overcome by the amendments herein, which restrict the definition of  $R_5$  to a substituted or unsubstituted heterocyclic group selected from furyl, thienyl, pyrrolyl, pyranlyl, thiopyranlyl, pyridyl, thiazolyl, imidazolyl, pyrimidyl, triazinyl, indolyl, quinolyl, purinyl and benzothiazolyl. A compound of formula (I) having  $R_5$  defined as one of the above-named heterocyclic groups is neither disclosed nor suggested by Badger. Accordingly, it is respectfully submitted that Claims 6 - 17 as amended are not anticipated by and would not have been obvious over Badger.

Rejection of Claims 6, 7, 10, 11, 14 and 15 under 35 U.S.C.

§102(b) over Kamoun et al

Claims 6, 7, 10, 11, 14 and 15 were rejected under 35 U.S.C. §102(b) as anticipated by Kamoun et al. The Examiner states that Kamoun et al teaches the administration of the compound 1,3,7-trimethyl-8[3-(4-diethylaminocarbonyl piperazino)propyl]xanthine hydrochloride, which the Examiner alleges is a compound of Formula (I), to treat Alzheimer's disease.

It is respectfully submitted that this rejection is overcome by the amendments herein, which restrict the definition of R<sub>5</sub> to a substituted or unsubstituted heterocyclic group, selected from furyl, thienyl, pyrrolyl, pyranlyl, thiopyranlyl, pyridyl, thiazolyl, imidazolyl, pyrimidyl, triazinyl, indolyl, quinolyl, purinyl and benzothiazolyl. A compound of formula (I) having R<sub>5</sub> defined as one of the above-named heterocyclic groups is neither disclosed nor suggested by Kamoun et al. Accordingly, it is respectfully submitted that Claims 6, 7, 10, 11, 14 and 15 as amended are not anticipated by and would not have been obvious over Kamoun et al.

#### Conclusion

In view of the foregoing amendments and remarks, it is respectfully submitted that Claims 6 - 17 are in condition for allowance. Favorable reconsideration is respectfully requested.

To the extent necessary, Applicants petition for an extension of time under 37 CFR § 1.136. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to the Deposit Account No. 01-2135 (Case No. 506.38266X00) and please credit any excess fees to such Deposit Account.

Respectfully submitted,

ANTONELLI, TERRY, STOUT & KRAUS, LLP



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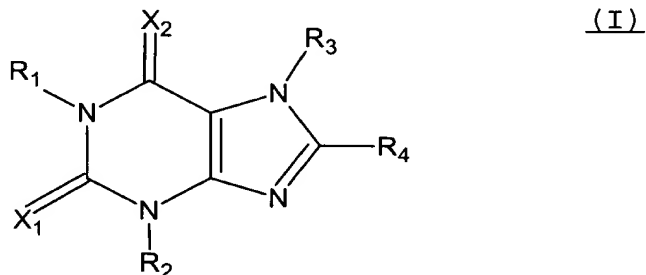
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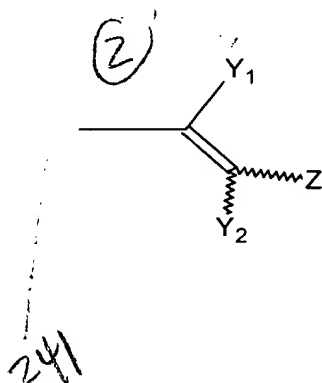
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IN THE CLAIMS

6. (amended) A method of inhibiting neurodegeneration, which comprises administering an effective dose of a xanthine derivative represented by formula ~~(I)~~ (I):

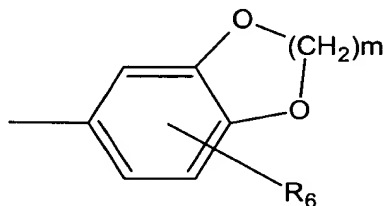


wherein  $X_1$  and  $X_2$  independently represent O or S,  $R_1$ ,  $R_2$  and  $R_3$  independently represent hydrogen, lower alkyl, lower alkenyl or lower alkynyl;  $R_4$  represents ~~cycloalkyl,  $-(CH_2)_n$  wherein  $n$  is an integer of 0 to 4,  $-(CH_2)_n-R_5$ , wherein  $R_5$  represents substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group, selected from furyl, thienyl, pyrrolyl, pyranyl, thiopyranyl, pyridyl, thiazolyl, imidazolyl, pyrimidyl, triazinyl, indolyl, quinolyl, purinyl and benzothiazolyl, and  $n$  is an integer of 0 to 4, or the following group:~~



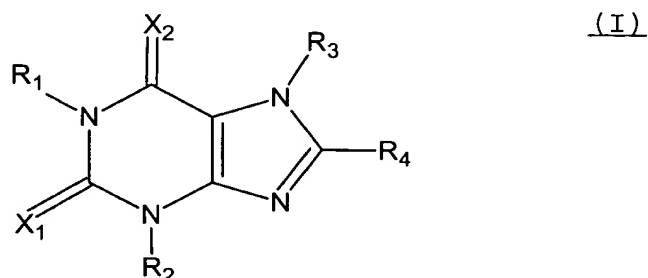
this is  
 $R_4$

wherein  $Y_1$  and  $Y_2$  independently represent hydrogen, halogen or lower alkyl, and Z represents substituted or unsubstituted aryl, or the following group:

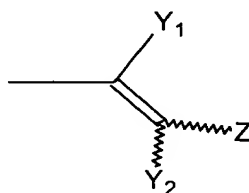


wherein  $m$  is an integer of 1 to 3 and  $R_6$  represents hydrogen, hydroxy, lower alkyl, lower alkoxy, halogen, nitro or amino, or a substituted or unsubstituted heterocyclic group selected from furyl and pyridyl; and wherein the substituted aryl and the substituted heterocyclic group have 1 to 3 independently-selected substituents selected from the group consisting of lower alkyl, hydroxy, lower alkoxy or lower alkoxy substituted with a substituent(s) selected from the group consisting of hydroxy, lower alkoxy, halogen, amino, azido, carboxy and lower alkoxycarbonyl, halogen, nitro, amino, lower alkylamino, di(lower alkyl)amino, trifluoromethyl, tri-fluoromethoxy, benzyloxy, phenyl, phenoxy, lower alkanoyl, lower alkanoyloxy, aroyloxy, aralkanoyloxy, carboxy, lower alkoxycarbonyl, lower alkylcarbamoyl, di(lower alkyl)-carbamoyl, sulfo, lower alkoxysulfonyl, lower alkylsulfamoyl and di(lower alkyl)sulfamoyl; or a pharmaceutically acceptable salt thereof, as an active ingredient.

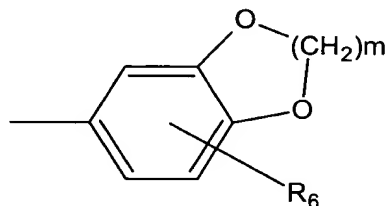
10. (amended) A method of treating neurodegenerative disorders except for Parkinson's disease and attention deficit hyperactivity disorder, which method comprises administering an effective dose of a xanthine derivative represented by formula (I):



wherein X<sub>1</sub> and X<sub>2</sub> independently represent O or S, R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> independently represent hydrogen, lower alkyl, lower alkenyl or lower alkynyl; R<sub>4</sub> represents ~~cycloalkyl, -(CH<sub>2</sub>)<sub>n</sub> wherein n is an integer of 0 to 4,~~ -(CH<sub>2</sub>)<sub>n</sub>-R<sub>5</sub>, wherein R<sub>5</sub> represents substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group, selected from furyl, thienyl, pyrrolyl, pyranyl, thiopyranyl, pyridyl, thiazolyl, imidazolyl, pyrimidyl, triazinyl, indolyl, quinolyl, purinyl and benzothiazolyl, and n is an integer of 0 to 4, or the following group:

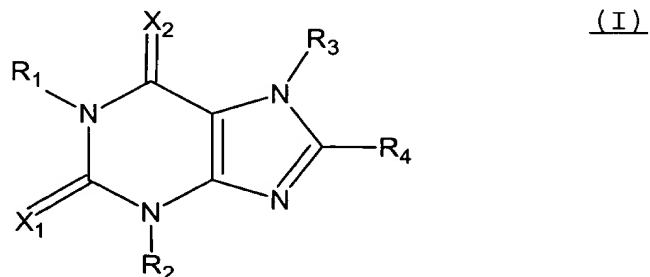


wherein  $Y_1$  and  $Y_2$  independently represent hydrogen, halogen or lower alkyl, and Z represents substituted or unsubstituted aryl, or the following group:

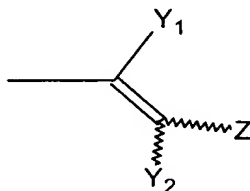


wherein  $m$  is an integer of 1 to 3 and  $R_6$  represents hydrogen, hydroxy, lower alkyl, lower alkoxy, halogen, nitro or amino, or a substituted or unsubstituted heterocyclic group selected from furyl and pyridyl; and wherein the substituted aryl and the substituted heterocyclic group have 1 to 3 independently-selected substituents selected from the group consisting of lower alkyl, hydroxy, lower alkoxy or lower alkoxy substituted with a substituent(s) selected from the group consisting of hydroxy, lower alkoxy, halogen, amino, azido, carboxy and lower alkoxycarbonyl, halogen, nitro, amino, lower alkylamino, di(lower alkyl)amino, trifluoromethyl, tri-fluoromethoxy, benzyloxy, phenyl, phenoxy, lower alkanoyl, lower alkanoyloxy, aroyloxy, aralkanoyloxy, carboxy, lower alkoxycarbonyl, lower alkylcarbamoyl, di(lower alkyl)-carbamoyl, sulfo, lower alkoxysulfonyl, lower alkylsulfamoyl and di(lower alkyl)sulfamoyl; or a pharmaceutically acceptable salt thereof, as an active ingredient.

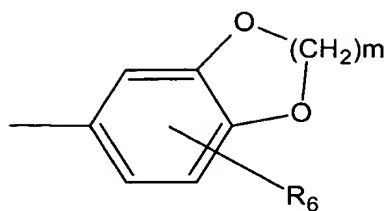
14. (amended) A method of treating Alzheimer's disease, which comprises administering an effective dose of the xanthine derivative represented by formula (I):



wherein  $X_1$  and  $X_2$  independently represent O or S,  $R_1$ ,  $R_2$  and  $R_3$  independently represent hydrogen, lower alkyl, lower alkenyl or lower alkynyl;  $R_4$  represents ~~cycloalkyl,  $-(CH_2)_n$  wherein n is an integer of 0 to 4,~~  $-(CH_2)_n-R_5$ , wherein  $R_5$  represents ~~substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group,~~ selected from furyl, thienyl, pyrrolyl, pyranyl, thiopyranyl, pyridyl, thiazolyl, imidazolyl, pyrimidyl, triazinyl, indolyl, quinolyl, purinyl and benzothiazolyl, and n is an integer of 0 to 4, or the following group:



wherein  $Y_1$  and  $Y_2$  independently represent hydrogen, halogen or lower alkyl, and Z represents substituted or unsubstituted aryl, or the following group:



wherein  $m$  is an integer of 1 to 3 and  $R_6$  represents hydrogen, hydroxy, lower alkyl, lower alkoxy, halogen, nitro or amino, or a substituted or unsubstituted heterocyclic group selected from furyl and pyridyl; and wherein the substituted aryl and the substituted heterocyclic group have 1 to 3 independently-selected substituents selected from the group consisting of lower alkyl, hydroxy, lower alkoxy or lower alkoxy substituted with a substituent(s) selected from the group consisting of hydroxy, lower alkoxy, halogen, amino, azido, carboxy and lower alkoxy carbonyl, halogen, nitro, amino, lower alkylamino, di(lower alkyl)amino, trifluoromethyl, tri-fluoromethoxy, benzyloxy, phenyl, phenoxy, lower alkanoyl, lower alkanoyloxy, aroyloxy, aralkanoyloxy, carboxy, lower alkoxy carbonyl, lower alkyl carbamoyl, di(lower alkyl)-carbamoyl, sulfo, lower alkoxy sulfonyl, lower alkyl sulfamoyl and di(lower alkyl) sulfamoyl; or a pharmaceutically acceptable salt thereof, as an active ingredient.